

=> d his

(FILE 'HOME' ENTERED AT 09:19:32 ON 01 FEB 2007)

FILE 'REGISTRY' ENTERED AT 09:20:06 ON 01 FEB 2007

ACT KIS374A/A
 L1 STR
 L2 SCR 1950 AND 1994
 L3 SCR 1363 OR 1236
 L4 SCR 1838
 L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
 L6 STR
 L7 9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

FILE 'HCAPLUS' ENTERED AT 09:20:32 ON 01 FEB 2007

E US20050095280/PN
 L8 1 S E3
 SEL RN

FILE 'REGISTRY' ENTERED AT 09:21:20 ON 01 FEB 2007

L9 12 S E1-E12

FILE 'HCAPLUS' ENTERED AT 09:21:29 ON 01 FEB 2007

L10 1 S L8 AND L9

FILE 'REGISTRY' ENTERED AT 09:21:45 ON 01 FEB 2007

L11 4 S L9 AND L7

FILE 'HCAPLUS' ENTERED AT 09:22:02 ON 01 FEB 2007

L12 7 S L7
 L13 25 S SAVVA M?/AU
 L14 10 S L13 AND LIPID?
 L15 6 S L12 NOT L14

FILE 'USPATFULL' ENTERED AT 09:26:53 ON 01 FEB 2007

L16 3 S L7
 L17 2 S L14
 L18 2 S L16 NOT L17

FILE 'TOXCENTER' ENTERED AT 09:27:40 ON 01 FEB 2007

L19 4 S L7
 L20 1 S L14
 L21 4 S L19 NOT L20

FILE 'HCAPLUS' ENTERED AT 09:32:00 ON 01 FEB 2007

=> d que nos l14

L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
 L14 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND LIPID?

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 09:35:18 ON 01 FEB 2007

CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 30 Jan 2007 (20070130/PD)

FILE LAST UPDATED: 30 Jan 2007 (20070130/ED)

HIGHEST GRANTED PATENT NUMBER: US7171694

HIGHEST APPLICATION PUBLICATION NUMBER: US2007022507

CA INDEXING IS CURRENT THROUGH 30 Jan 2007 (20070130/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 30 Jan 2007 (20070130/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

=> d que nos l17

L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L17 2 SEA FILE=USPATFULL ABB=ON PLU=ON L13 AND LIPID?

=> file toxcenter

FILE 'TOXCENTER' ENTERED AT 09:35:31 ON 01 FEB 2007
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FILE COVERS 1907 TO 30 Jan 2007 (20070130/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The MEDLINE file segment has been updated with 2007 MeSH terms.and
See HELP RLOAD for details.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2007 vocabulary.

=> d que nos l20

L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L20 1 SEA FILE=TOXCENTER ABB=ON PLU=ON L13 AND LIPID?

=> file hcaplus uspatfull toxcenter

FILE 'HCAPLUS' ENTERED AT 09:35:54 ON 01 FEB 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 09:35:54 ON 01 FEB 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 09:35:54 ON 01 FEB 2007
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=> dup rem l14 l17 l20

PROCESSING COMPLETED FOR L14
PROCESSING COMPLETED FOR L17
PROCESSING COMPLETED FOR L20
L22 10 DUP REM L14 L17 L20 (3 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE HCAPLUS

=> d ibib ed ab 1-10

L22 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:394541 HCAPLUS Full-text

DOCUMENT NUMBER: 142:435781

TITLE: Single-component pH-sensitive liposomes of
reduced solid-to-liquid phase transition
temperatures for gene delivery

INVENTOR(S): Savva, Michalakis

PATENT ASSIGNEE(S): Michalakis Savva, USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005095280	A1	20050505	US 2003-686374	

200310

15

PRIORITY APPLN. INFO.:

US 2003-686374

200310

15

OTHER SOURCE(S): MARPAT 142:435781

ED Entered STN: 09 May 2005

AB The current invention relates to the synthesis of novel cationic lipids and their use as delivery vectors for nucleic acids, peptides and other synthetic drugs, in vitro and in vivo. The cationic lipids described herein form stable lamellar structures (liposomes) at physiol. pH but destabilize to micelles at acidic and alkaline pH. These structures are characterized by high elasticity, increased fluidity and high transfection activity relative to the corresponding 1,2-dialkyl cationic derivs. and other phospholipids analogs.

L22 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:346678 HCAPLUS Full-text

DOCUMENT NUMBER: 142:417187

TITLE: Cationic lipids for nucleic acid delivery

INVENTOR(S): Savva, Michalakis

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005084522	A1	20050421	US 2003-686262	200310 15

PRIORITY APPLN. INFO.:

US 2003-686262

200310

15

OTHER SOURCE(S): MARPAT 142:417187

ED Entered STN: 22 Apr 2005

AB The invention describes the synthetic methods for a series of pH-sensitive cationic lipids with diamido linkages between the 1,2-diamino-3-propanol backbone and the hydrocarbon chains. Their in vitro biol. activity of the resulting lipid-DNA complexes is also described.

L22 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2003:423359 HCAPLUS Full-text

DOCUMENT NUMBER: 140:88218

TITLE: In vitro lipofection with novel series of symmetric 1,3-dialkoylamidopropane-based cationic surfactants containing single primary and tertiary amine polar head groups

AUTHOR(S): Sheikh, Mohammad; Feig, Jennifer; Gee, Becky; Li, Song; Savva, Michalakis

CORPORATE SOURCE: Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Division of Pharmaceutics, Long Island University, Brooklyn, NY, 11201, USA

SOURCE: Chemistry and Physics of Lipids (2003), 124(1), 49-61

CODEN: CPLIA4; ISSN: 0009-3084

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 03 Jun 2003

AB A novel series of sym. double-chained primary and tertiary 1,3-dialkoylamido monovalent cationic lipids were synthesized and evaluated for their transfection activities. In the absence of the helper lipid DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the primary and tertiary dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp. elicited transfection activity. This is a striking difference between sym. 1,2-diacyl glycerol-based monovalent cationic lipids that always found both dioleoyl and dimyristoyl analogs being efficient transfection reagents. In the presence of helper lipid, all cationic derivs. induced marker gene expression, except the dilauroyl analogs 1,3lmp1 and 1,3lmt1 that elicited no transfection activity. Combining electrophoretic mobility data of the lipoplexes at different charge ratios with transfection activity suggested two requirements for high transfection activity with monovalent double-chained cationic lipids, i.e., binding/association of the lipid to the plasmid DNA and membrane fusion properties of the lipid layers surrounding the DNA.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1162755 HCAPLUS Full-text

DOCUMENT NUMBER: 144:74592

TITLE: In Vitro Lipofection with Novel Asymmetric
Series of 1,2-Dialkoylamidopropane-Based
Cytofectins Containing Single Symmetric
Bis-(2-dimethylaminoethane) Polar Headgroups
AUTHOR(S): Savva, Michalakos; Chen, Pensung;
Aljaberi, Ahmad; Selvi, Bilge; Spelios, Michael
CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold
Marie Schwartz College of Pharmacy and Health
Sciences, Long Island University, Brooklyn, NY,
11201, USA

SOURCE: Bioconjugate Chemistry (2005), 16(6), 1411-1422
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 01 Nov 2005

AB Novel N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl[bis-(2-dimethylaminoethane)] bivalent cationic lipids were synthesized and evaluated for in vitro transfection activity against a murine melanoma cell line. In the absence of the helper lipid DOPE (1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), only the dioleoyl derivative 22 (1,2lb5) elicited transfection activity. The transfection activity of this lipid was reduced when formulated with DOPE. Contrary to that, the dimyristoyl derivative 19 (1,2lb2) mediated no activity when used alone but induced the highest levels of marker gene expression in the presence of DOPE. In an effort to correlate the transfection activity with cationic lipid structures, the physicochem. properties of cationic lipids in isolation and of lipoplexes were studied with surface tensiometry, photon correlation spectroscopy, gel electrophoresis mobility shift assay, and fluorescence techniques. In regard to the lipoplex properties, gel electrophoresis mobility shift assay and EtBr exclusion fluorescence assay revealed that the 1,2lb5 was the only lipid to associate and condense plasmid DNA, resp. Photon correlation spectroscopy anal. found that 1,2lb5/DNA complexes were of relatively small size compared to all other lipoplexes. With respect to the properties of isolated lipids, Langmuir monolayer studies and fluorescence anisotropy on cationic lipid dispersions verified high two-plane elasticity and increased fluidity of the transfection competent dioleoyl derivative 1,2lb5, resp. The results indicate that high transfection activity is mediated by cationic lipids characterized by an expanded mean mol. area, high mol. elasticity, and increased fluidity.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:25928 HCAPLUS Full-text

DOCUMENT NUMBER: 143:272152

TITLE: Synthesis, in vitro transfection activity and
physicochemical characterization of novel

N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl-
 (dimethylaminoethane) amphiphilic derivatives
 AUTHOR(S): Aljaberi, Ahmad; Chen, Pensung; Savva,
 Michalakakis
 CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and
 Marie Schwartz College of Pharmacy and Health
 Sciences, Long Island University, Brooklyn, NY,
 11201, USA
 SOURCE: Chemistry and Physics of Lipids (2005), 133(2),
 135-149
 CODEN: CPLIA4; ISSN: 0009-3084
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 Jan 2005
 AB A novel series of N,N'-diacyl-1,2-diaminopropyl-3-carbamoyl- (dimethylaminoethane)
 cationic derivs. was synthesized and screened for in vitro transfection activity at
 different charge ratios in the presence and absence of the helper lipids DOPE and
 cholesterol. Physicochem. properties of lipid-DNA complexes were studied by gel
 electrophoresis, fluorescence spectroscopy and dynamic light scattering. The
 interfacial properties of the lipids in isolation were studied using the Langmuir film
 balance technique at 23 °C. It was found that only lipoplexes formulated with the
 dioleoyl derivative, 1,2lmt[5], mediated significant in vitro transfection activity.
 Optimum activity was obtained with 1,2lmt[5]/DOPE mixture at a \pm charge ratio of 2. In
 agreement with the transfection results, 1,2lmt[5] was the only lipid found to complex
 and retard DNA migration as verified by gel electrophoresis. Despite the efficient
 complexation, no significant condensation of plasmid DNA was observed as indicated by
 fluorescence spectroscopy measurements. Monolayer studies showed that the dioleoyl
 derivative 1,2lmt[5] was the only lipid that existed in an all liquid-expanded state
 with a collapse area and collapse pressure of 59.5 Å² and 38.7 mN/m, resp. This lipid
 was also found to have the highest elasticity with a compressibility modulus at
 monolayer collapse of 80.4 mN/m. In conclusion, increased acyl chain fluidity and high
 mol. elasticity of cationic lipids were found to correlate with improved transfection
 activity.
 REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE
 IN THE RE FORMAT
 L22 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2005:503242 HCAPLUS Full-text
 DOCUMENT NUMBER: 144:198343
 TITLE: Correlation of the physicochemical properties of
 symmetric 1,3-dialkylamidopropane-based
 cationic lipids containing single
 primary and tertiary amine polar head groups
 with in vitro transfection activity
 AUTHOR(S): Savva, Michalakakis; Aljaberi, Ahmad;
 Feig, Jennifer; Stolz, Donna Beer
 CORPORATE SOURCE: Division of Pharmaceutical Sciences, Arnold and
 Marie Schwartz College of Pharmacy and Health
 Sciences, Long Island University, Brooklyn, NY,
 11201, USA
 SOURCE: Colloids and Surfaces, B: Biointerfaces (2005),
 43(1), 43-56
 CODEN: CSBBEQ; ISSN: 0927-7765
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 13 Jun 2005
 AB The physicochem. properties of a novel series of sym. 1,3-dialkylamidopropane-based
 cationic amphiphiles [M. Sheikh, J. Feig, B. Gee, S. Li, M. Savva, In vitro lipofection
 with novel series of sym. 1,3-dialkylamidopropane-based cationic surfactants
 containing single primary and tertiary amine polar head groups, Chemical Phys. Lipids
 124 (2003) 49-61] were studied by several techniques, in an effort to correlate
 cationic lipid structure with transfection efficacy. It was found that only the
 unsubstituted amine and tertiary amine dioleoyl derivs. 1,3lmp5 and 1,3lmt5, resp.,
 mediated in vitro transfection activity in the absence of helper lipids. This activity

pattern was consistent with ethidium bromide fluorescence quenching studies, which indicated that only these two derivs. bound to and efficiently condense plasmid DNA at physiol. pH. Dynamic light scattering indicated that lipoplexes made by these two cationic lipids were relatively small particles below 1 μ m, in sharp contrast to lipoplexes bigger than 3 μ m composed of saturated cationic derivs. Transmission electron microscopy studies clearly indicated that cationic lipid dispersions made by saturated derivs. form multilamellar tubules at physiol. pH. Calorimetric studies showed that cationic amphiphiles with saturated acyl chains longer than 12 carbons exhibit solid-to-liquid crystalline phase transitions above 37 °C. In agreement with the microscopy and calorimetry studies, Langmuir film balance expts. indicated that saturated derivs. with hydrophobic chains longer than 12 carbons are not well hydrated and exist at a chain-ordered state at ambient temperature. Calcn. of compressibility moduli from monolayer compression isotherms at 23 °C suggested that monolayers made by cationic lipids bearing saturated acyl chains are less compressible relative to those of the dioleoyl derivs. 1,3lmp5 and 1,3lmt5. In conclusion, high hydration, increased fluidity and high elasticity of cationic lipid assemblies in isolation, all correlate with high in vitro transfection activity.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:647605 HCAPLUS Full-text
DOCUMENT NUMBER: 132:46579
TITLE: Effect of PEG homopolymer and grafted
amphiphilic PEG-palmityl on the thermotropic
phase behavior of 1,2-dipalmitoyl-sn-glycero-3-
phosphocholine bilayer
AUTHOR(S): Savva, Michalakis; Huang, Leaf
CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
Pharmacology, University of Pittsburgh,
Pittsburgh, PA, 15261, USA
SOURCE: Journal of Liposome Research (1999), 9(3),
357-365
CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 12 Oct 1999

AB Phospholipids covalently attached to polyethylene glycol (PEG-PE) are routinely used for the preparation of long-circulating liposomes. The common preparation procedure for long-circulating liposomes involves use of organic solvent. Although there is a plethora of studies describing the interaction of PEG-PE with bilayers, little is known about the effects of PEG homopolymers and single chain amphiphilic PEG on liposome structure. In the present investigation the interaction of PEG homopolymer and amphiphilic PEG-palmityl conjugate with large multilamellar liposomes composed of 1,2-dipalmitoyl-sn-glycero-phosphocholine was investigated utilizing differential scanning calorimetry. Vesicle and aggregate sizes were determined by dynamic light scattering. DSC thermograms revealed interaction of PEG homopolymer with DPPC when the two are premixed in organic solvent. The data suggest that PEG interacts with the phospholipid acyl chains deep in the bilayer. Several questions are raised regarding the suitability of the current procedure for preparation of long-circulating liposomes which utilizes organic solvent. Incorporation of only 2 mol% 5 kDa PEG-palmityl conjugate completely solubilized DPPC liposomes. Packing geometry of the lipid anchor, irrespectively of the polymer mol. weight, is suggested to be the primary factor for successful grafting of hydrophilic polymers on liposomes. Pure PEG-palmityl formed self-assembled organized structures of potential use in the delivery of poorly soluble drugs.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:502263 HCAPLUS Full-text
DOCUMENT NUMBER: 131:327399
TITLE: Effect of Grafted Amphiphilic PVP-Palmityl

Polymers on the Thermotropic Phase Behavior of
1,2 Dipalmitoyl-sn-glycero-3-phosphocholine
Bilayer

AUTHOR(S): Savva, Michalakis; Torchilin, Vladimir
P.; Huang, Leaf
CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
Pharmacology, University of Pittsburgh,
Pittsburgh, PA, 15261, USA
SOURCE: Journal of Colloid and Interface Science (1999),
217(1), 166-171
CODEN: JCISA5; ISSN: 0021-9797
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 12 Aug 1999

AB To better understand how grafted polymers interact with liposome membrane, a comparative study was conducted to investigate the influence of different chain length polyvinyl pyrrolidone-palmityl (PVP-p) conjugates on the thermotropic phase behavior of 1,2 dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC) bilayer. Lipid-polymer dispersions were prepared by mixing DPPC and variable concns. of PVP-p conjugates in chloroform. Hydration of lipids was performed at 50-55°C after complete elimination of the organic solvent. DSC was used to determine lipid miscibility and bilayer-polymer interactions. Particle size was determined by photon correlation spectroscopy. Increasing concns. of 6 kDa PVP-p caused a shift of the main phase transition of DPPC at lower temps. At 9.1 mol% the DPPC phase pretransition (Tp) is abolished. At 16.7 mol%, differential scanning calorimetry showed an endothermic phase transition at 24.9°C. The enthalpy of this transition was twice as high compared to the main phase transition enthalpy of pure DPPC. Inclusion of more than 20 mol% of 6 kDa PVP-p resulted in a complete bilayer micellization. Qual. similar to the 6 kDa were the results obtained with the 12 kDa PVP-p conjugate. Increasing concns. of 25 kDa PVP-p from 1 to 13 mol% resulted in a decrease of the main DPPC phase transition temperature. At 13 mol% the new mol. self-assembled structure as previously identified with the lower MW PVP-p conjugates also showed up at the DSC thermogram. However, in sharp contrast to the lower MW PVP-p conjugates, increasing the 25 kDa PVP-p content did not result in bilayer disruption; rather, it resulted in a bilayer stabilization. The consequences of the hydrophobically modified PVP interaction with the bilayer are considered neg. with respect to the long-circulating properties of liposomes in the blood. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:502262 HCAPLUS Full-text

DOCUMENT NUMBER: 131:327398

TITLE: Effect of Polyvinylpyrrolidone on the Thermal
Phase Transition of 1,2-Dipalmitoyl-sn-glycero-3-
phosphocholine Bilayer

AUTHOR(S): Savva, Michalakis; Torchilin, Vladimir
P.; Huang, Leaf

CORPORATE SOURCE: Departments of Pharmaceutical Sciences and
Pharmacology, University of Pittsburgh,
Pittsburgh, PA, 15261, USA

SOURCE: Journal of Colloid and Interface Science (1999),
217(1), 160-165
CODEN: JCISA5; ISSN: 0021-9797

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Aug 1999

AB The purpose of this study was to investigate the interaction of polyvinyl pyrrolidone (PVP) with phospholipid bilayers in an effort to add a new dimension to our understanding of polymer interaction with lipids. For the preparation of lipid-polymer dispersions, measured amts. of DPPC (1,2 dipalmitoyl-sn-glycero-3-phosphocholine) and PVP were mixed in chloroform. After complete elimination of organic solvent, the dry mixts. were hydrated at 50-55°C. Interactions between DPPC and PVP were assessed by DSC and photon correlation spectroscopy (PS). Separation of liposomes and micelles was

10/686374

performed by centrifugation. Liquid scintillation counting and a UV spectrophotometer were used for their anal. PVP added as dry powder or added as aqueous solution to dry lipid or preformed liposomes failed to interact. Only PVP previously dissolved in chloroform interacted with DPPC. The DPPC main phase transition moved to lower temps. with increasing PVP concns. This reduction of the phase transition temperature was accompanied by an increase of the DPPC phase transition enthalpy. Anal. of solubilization indicated that the amount of PVP present in the bilayer is dependent on the PVP bulk concentration. The data suggest interaction of PVP previously dissolved in chloroform with the acyl chains of the phospholipid deep into the bilayer. (c) 1999 Academic Press.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L22 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:481727 HCAPLUS Full-text
DOCUMENT NUMBER: 129:235495
TITLE: PVP: a "pretender" molecule
AUTHOR(S): Savva, M.; Torchilin, V. P.; Huang, L.
CORPORATE SOURCE: University of Pittsburgh, Pittsburgh, PA, 15261,
USA
SOURCE: Proceedings of the International Symposium on
Controlled Release of Bioactive Materials
(1998), 25th, 134-135
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Aug 1998

AB It appears that dipalmitoylphosphatidylcholine-PVP prepns. are stabilized through an enthalpic contribution. The observed lipid-polymer interaction is attributed to a change in the conformation of PVP, taking place during its dissoln. in organic solvent. Thus, PVP is a pretender mol. being able to acquire an appropriate conformation in a given environment. This can be of significant importance in formulations in which apolar solvents are used, e.g., transdermal and other topical dosage forms. In these formulations, the polymer might be presented in a hydrophobic conformation, thereby promoting keratinocyte barrier fluidization or interaction with living cells and other tissue components.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

=> d his nofile

(FILE 'HOME' ENTERED AT 09:19:32 ON 01 FEB 2007)

FILE 'REGISTRY' ENTERED AT 09:20:06 ON 01 FEB 2007
ACT KIS374A/A

L1 STR
L2 SCR 1950 AND 1994
L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307)SEA SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR
L7 9 SEA SUB=L5 SSS FUL L6

FILE 'HCAPLUS' ENTERED AT 09:20:32 ON 01 FEB 2007
E US20050095280/PN

L8 1 SEA ABB=ON PLU=ON US2005095280/PN
SEL RN

FILE 'REGISTRY' ENTERED AT 09:21:20 ON 01 FEB 2007

L9 12 SEA ABB=ON PLU=ON (112-64-1/BI OR 124-40-3/BI OR

10/686374

138404-83-8/BI OR 40538-81-6/BI OR 616-29-5/BI OR
642475-14-7/BI OR 7693-46-1/BI OR 821-48-7/BI OR
850785-34-1/BI OR 850785-35-2/BI OR 850785-36-3/BI OR
850785-37-4/BI)

L10 FILE 'HCAPLUS' ENTERED AT 09:21:29 ON 01 FEB 2007
1 SEA ABB=ON PLU=ON L8 AND L9

L11 FILE 'REGISTRY' ENTERED AT 09:21:45 ON 01 FEB 2007
4 SEA ABB=ON PLU=ON L9 AND L7

L12 FILE 'HCAPLUS' ENTERED AT 09:22:02 ON 01 FEB 2007
7 SEA ABB=ON PLU=ON L7
L13 25 SEA ABB=ON PLU=ON SAVVA M?/AU
L14 10 SEA ABB=ON PLU=ON L13 AND LIPID?
L15 6 SEA ABB=ON PLU=ON L12 NOT L14

L16 FILE 'USPATFULL' ENTERED AT 09:26:53 ON 01 FEB 2007
3 SEA ABB=ON PLU=ON L7
L17 2 SEA ABB=ON PLU=ON L13 AND LIPID?
L18 2 SEA ABB=ON PLU=ON L16 NOT L17

L19 FILE 'TOXCENTER' ENTERED AT 09:27:40 ON 01 FEB 2007
4 SEA ABB=ON PLU=ON L7
L20 1 SEA ABB=ON PLU=ON L13 AND LIPID?
L21 4 SEA ABB=ON PLU=ON L19 NOT L20

FILE 'HCAPLUS' ENTERED AT 09:32:00 ON 01 FEB 2007
D SCAN L10 TI
D QUE NOS L14

FILE 'USPATFULL' ENTERED AT 09:35:18 ON 01 FEB 2007
D QUE NOS L17

FILE 'TOXCENTER' ENTERED AT 09:35:31 ON 01 FEB 2007
D QUE NOS L20

FILE 'HCAPLUS, USPATFULL, TOXCENTER' ENTERED AT 09:35:54 ON 01 FEB 2007
L22 10 DUP REM L14 L17 L20 (3 DUPLICATES REMOVED)
ANSWERS '1-10' FROM FILE HCAPLUS
D IBIB ED AB 1-10

FILE 'REGISTRY' ENTERED AT 09:36:38 ON 01 FEB 2007
D QUE STAT L7

FILE 'HCAPLUS' ENTERED AT 09:36:53 ON 01 FEB 2007
D QUE NOS L15

FILE 'USPATFULL' ENTERED AT 09:37:31 ON 01 FEB 2007
D QUE NOS L18

FILE 'TOXCENTER' ENTERED AT 09:37:44 ON 01 FEB 2007
D QUE NOS L21

FILE 'HCAPLUS, USPATFULL, TOXCENTER' ENTERED AT 09:38:20 ON 01 FEB 2007
L23 8 DUP REM L15 L18 L21 (4 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE HCAPLUS
ANSWERS '7-8' FROM FILE USPATFULL
D IBIB ED ABS HITSTR 1-8

FILE 'HCAPLUS' ENTERED AT 09:39:52 ON 01 FEB 2007
D QUE NOS L14

FILE 'USPATFULL' ENTERED AT 09:40:37 ON 01 FEB 2007
D QUE NOS L17

FILE 'TOXCENTER' ENTERED AT 09:40:56 ON 01 FEB 2007
D QUE NOS L20

FILE 'REGISTRY' ENTERED AT 09:41:10 ON 01 FEB 2007
D QUE STAT L7

FILE 'HCAPLUS' ENTERED AT 09:41:23 ON 01 FEB 2007
D QUE NOS L15

FILE 'USPATFULL' ENTERED AT 09:41:52 ON 01 FEB 2007
D QUE NOS L18

FILE 'TOXCENTER' ENTERED AT 09:42:24 ON 01 FEB 2007
D QUE NOS L21

=> file reg

FILE 'REGISTRY' ENTERED AT 09:36:38 ON 01 FEB 2007
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STRUCTURE FILE UPDATES: 31 JAN 2007 HIGHEST RN 918932-71-5
DICTIONARY FILE UPDATES: 31 JAN 2007 HIGHEST RN 918932-71-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d que stat l7

L1 STR

N Ak N
1 2 3

Ak 4 Ak 5

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 2
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 2 4 5
GGCAT IS SAT AT 2
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M11 C AT 4
ECOUNT IS M11 C AT 5

GRAPH ATTRIBUTES:

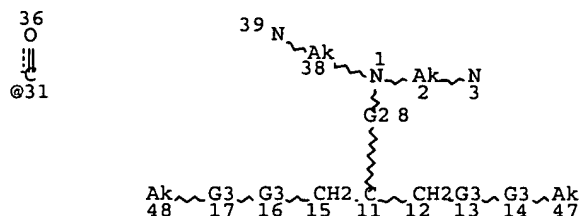
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 5

STEREO ATTRIBUTES: NONE

L2 SCR 1950 AND 1994

10/686374

L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR



REP G2=(1-4) A
VAR G3=CH2/31/NH/S/O
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 2
CONNECT IS E2 RC AT 38
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 2 38 47 48
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M11 C AT 47
ECOUNT IS M11 C AT 48

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L7 9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

100.0% PROCESSED 3288 ITERATIONS
SEARCH TIME: 00.00.01

9 ANSWERS

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 09:36:53 ON 01 FEB 2007
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FILE COVERS 1907 - 1 Feb 2007 VOL 146 ISS 6
FILE LAST UPDATED: 31 Jan 2007 (20070131/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos l15
L1 STR
L2 SCR 1950 AND 1994

10/686374

L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR
L7 9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L12 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L7
L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L14 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND LIPID?
L15 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 NOT L14

=> file uspatfull

FILE 'USPATFULL' ENTERED AT 09:37:31 ON 01 FEB 2007

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 30 Jan 2007 (20070130/PD)

FILE LAST UPDATED: 30 Jan 2007 (20070130/ED)

HIGHEST GRANTED PATENT NUMBER: US7171694

HIGHEST APPLICATION PUBLICATION NUMBER: US2007022507

CA INDEXING IS CURRENT THROUGH 30 Jan 2007 (20070130/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 30 Jan 2007 (20070130/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2006

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2006

=> d que nos l18

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L2 SCR 1950 AND 1994
L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR
L7 9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L16 3 SEA FILE=USPATFULL ABB=ON PLU=ON L7
L17 2 SEA FILE=USPATFULL ABB=ON PLU=ON L13 AND LIPID?
L18 2 SEA FILE=USPATFULL ABB=ON PLU=ON L16 NOT L17

=> file toxcenter

FILE 'TOXCENTER' ENTERED AT 09:37:44 ON 01 FEB 2007

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FILE COVERS 1907 TO 30 Jan 2007 (20070130/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The MEDLINE file segment has been updated with 2007 MeSH terms.and
See HELP RLOAD for details.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2007 vocabulary.

=> d que nos l21

L1 STR
L2 SCR 1950 AND 1994
L3 SCR 1363 OR 1236
L4 SCR 1838
L5 (3307)SEA FILE=REGISTRY SSS FUL L1 AND L2 AND L3 NOT L4
L6 STR
L7 9 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L13 25 SEA FILE=HCAPLUS ABB=ON PLU=ON SAVVA M?/AU
L19 4 SEA FILE=TOXCENTER ABB=ON PLU=ON L7
L20 1 SEA FILE=TOXCENTER ABB=ON PLU=ON L13 AND LIPID?
L21 4 SEA FILE=TOXCENTER ABB=ON PLU=ON L19 NOT L20

=> file hcaplus uspatfull toxcenter
 FILE 'HCAPLUS' ENTERED AT 09:38:20 ON 01 FEB 2007
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FILE 'USPATFULL' ENTERED AT 09:38:20 ON 01 FEB 2007
 CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 09:38:20 ON 01 FEB 2007
 COPYRIGHT (C) 2007 ACS

=> dup rem l15 l18 l21
 PROCESSING COMPLETED FOR L15
 PROCESSING COMPLETED FOR L18
 PROCESSING COMPLETED FOR L21
 L23 8 DUP REM L15 L18 L21 (4 DUPLICATES REMOVED)
 ANSWERS '1-6' FROM FILE HCAPLUS
 ANSWERS '7-8' FROM FILE USPATFULL

=> d ibib ed abs hitstr 1-8

L23 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
 ACCESSION NUMBER: 2006:259279 HCAPLUS Full-text
 DOCUMENT NUMBER: 145:152309
 TITLE: Optimized lipopolyplex formulations for gene transfer to human colon carcinoma cells under in vitro conditions
 AUTHOR(S): Pelisek, Jaroslav; Gaedtke, Lars; DeRouchey, Jason; Walker, Greg F.; Nikol, Sigrid; Wagner, Ernst
 CORPORATE SOURCE: Department of Pharmacy, Center of Drug Research, Pharmaceutical Biology-Biotechnology, Ludwig Maximilian University, Munich, Germany
 SOURCE: Journal of Gene Medicine (2006), 8(2), 186-197
 CODEN: JGMEFG; ISSN: 1099-498X
 PUBLISHER: John Wiley & Sons Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

ED Entered STN: 21 Mar 2006

AB Polycation (PC, polyplex), cationic lipid (CL, lipoplex), and a combination of PC/CL (lipopolyplex) formulations were investigated for gene transfer to slow-proliferating human colon carcinoma cell lines (COGA). The luciferase reporter gene was complexed with either PC, CL, or PC/CL. PCs included linear (PEI22lin, 22 kDa) and branched polyethylenimine (PEI2k, 2 kDa; PEI25br, 25 kDa) and poly-L-lysine (PLL18 with 18 lysine monomers). CLs included DOCSPER, DOSPER and DOTAP. Lipopolyplexes were formed by either sequentially first mixing DNA with PC or CL, followed by addition of CL or PC, resp., or simultaneously with both PC and CL. Particle size and zeta-potential were determined and gene transfer and cytotoxicity were quantified on COGA-3. The highest gene transfer was achieved when DNA was first complexed with PC followed by CL. At low ionic strength, particles were small (50-130 nm) with a zeta-potential of +20-40 mV. At physiol. ionic strength, only lipopolyplexes of DOCSPER or DOSPER and their resp. lipopolyplexes with PEI25br were stable to aggregation (140-220 nm). Lipopolyplexes of PEI25br were between 5- to 400-fold more efficient compared to the corresponding lipopolyplexes or polyplexes in all cases. Chloroquine did not significantly affect lipopolyplex-mediated gene transfer. Thus, lipopolyplex formulations of PEI25br in combination with multivalent CLs (DOCSPER, DOSPER) are promising tools for in vitro and potentially also in vivo gene transfer to colorectal cancer cells.

IT 203188-43-6

RL: ADV (Adverse effect, including toxicity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (optimized lipopolyplex formulations for gene transfer to human colon carcinoma cells under in vitro conditions)

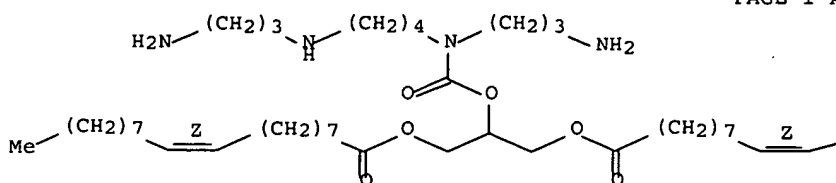
RN 203188-43-6 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)(4-[(3-

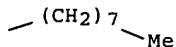
aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L23 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2006:143562 HCAPLUS Full-text

DOCUMENT NUMBER: 144:445618

TITLE: Local gene transfer of C-type natriuretic
peptide reduces restenosis and promotes
proliferation of endothelial cells

AUTHOR(S): Kuehn, A.; Pelisek, J.; Kopp, R.; Rolland, P.;
Jauch, K.-W.; Nikol, S.

CORPORATE SOURCE: Chirurgische Klinik und Poliklinik Grosshadern,
Ludwig-Maximilians-Universitaet, Munich, Germany

SOURCE: Chirurgisches Forum fuer Experimentelle und
Klinische Forschung (2005) 1-2

CODEN: CFEKA7; ISSN: 0303-6227

PUBLISHER: Springer GmbH

DOCUMENT TYPE: Journal

LANGUAGE: German

ED Entered STN: 16 Feb 2006

AB C-type natriuretic peptide (CNP) reduces proliferation of smooth muscle cells (SMCs) and stimulates endothelial growth. The authors investigated the long-term therapeutic effects of adventitial liposome-mediated CNP gene or peptide application in a porcine restenosis model. For in vitro applications, primary cultures of porcine SMCs and endothelial cells (ECs) were used. Gene transfer was performed with cationic lipid DOCSPER. In vivo treatment of pig femoral arteries was adventitial using a needle injection catheter following balloon over-dilation in 11 pigs, 5 pigs served as controls. Arteries were then investigated using angiog., Evan's blue staining, histomorphometry, immunohistochem., PCR and RT-PCR at 3 wk or 3 mo. Using CNP gene transfer in vitro, $29 \pm 7\%$ reduction of cell proliferation in SMCs and $22 \pm 6\%$ enhancement of cellular growth in ECs was observed with minimal cytotoxicity of $5 \pm 2\%$. CNP peptide demonstrated in SMC $50 \pm 11\%$ reduction of cell proliferation with $30 \pm 6\%$ toxicity and $12 \pm 5\%$ enhancement of cellular growth of ECs without toxic effects. Three weeks following application in vivo Evan's blue staining demonstrated intactness of endothelium in controls and therapy groups. Minimal neointima formation was observed at 3 mo using CNP gene (CNP Plasmid $1.7 \pm 0.4\%$ restenosis, CNP protein $5.6 \pm 1.7\%$ restenosis, control $15.6 \pm 4.8\%$ restenosis; $p < 0.05$). Periadventitial liposome-mediated CNP gene transfer in vivo resulted in rapid endothelial repair and significant long-term reduction of neointimal formation and was superior over single CNP peptide

administration. Advantages of CNP are its physiolo. origin and simultaneous inhibition of SMC proliferation and promotion of EC growth.

IT 203188-43-6

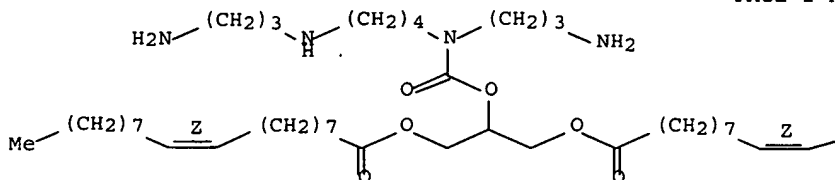
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(local gene transfer of C-type natriuretic peptide reduces restenosis and promotes proliferation of endothelial cells)

RN 203188-43-6 HCAPLUS

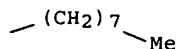
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:199221 HCAPLUS Full-text

DOCUMENT NUMBER: 137:57284

TITLE: Optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo

AUTHOR(S): Armeanu, Sorin; Pelisek, Jaroslav; Krausz, Eberhard; Fuchs, Alexandra; Groth, Detlef; Curth, Rene; Keil, Oliver; Quilici, Jacques; Rolland, Pierre H.; Reszka, Regina; Nikol, Sigrid

CORPORATE SOURCE: Medical Clinic I, Klinikum Grosshadern, Ludwig Maximilian University, Munich, D-81377, Germany

SOURCE: Molecular Therapy (2000), 1(4), 366-375
CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 19 Mar 2002

AB Gene therapy strategies for the prevention of restenosis postangioplasty are promising. Nonviral gene transfer to the arterial wall in vivo has so far been limited by poor efficiency. This study aimed to optimize transfection of primary vascular smooth muscle cells using cationic nonviral formulations based on cholesterol derivs. (DC-, DAC-, DCQ-, and Sp-Chol), double-chained amphiphiles (LipofectAMINE, DOTMA, DOSGA, DOSPER, and DOCSPER), or heterogeneous reagents (Superfect, Effectene, and Tfx-50). Estimation of transfection efficiencies was performed using galactosidase assays at different ratios of transfection reagent to plasmid DNA with reporter gene. Toxicity was monitored by analyzing cell metabolism Transfer efficiency and safety were determined

in a porcine restenosis model for local gene therapy using morphometry, histol., galactosidase assays, and reverse-transcriptase polymerase chain reaction. The highest in vitro transfection efficiency was achieved using the recently developed DOCSPER liposomes, with transfer rates of at least 20% in vascular smooth muscle cells. Transfer efficiency was further enhanced up to 20% by complexing with poly-L-lysine. Transfection efficiency in vivo in a porcine restenosis model was up to 15% of adventitial cells using DOCSPER vs. 0.1% using LipofectAMINE. Toxicity in vivo and in vitro was lowest using DOCSPER. Increased biol. effects were demonstrated following optimization of transfer conditions. (c) 2000 Academic Press.

IT 203188-43-6

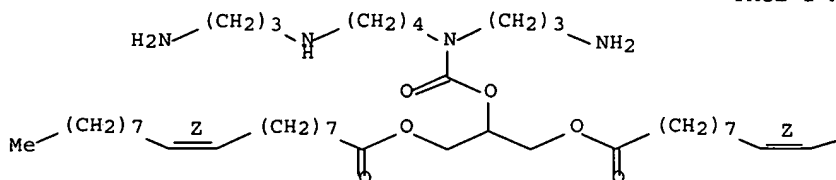
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization of nonviral gene transfer of vascular smooth muscle cells in vitro and in vivo)

RN 203188-43-6 HCAPLUS

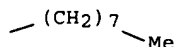
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1998:203964 HCAPLUS Full-text

DOCUMENT NUMBER: 128:326398

TITLE: Preparation and characterization of a new lipospermine for gene delivery into various cell-lines

AUTHOR(S): Groth, Detlef; Keil, Oliver; Lehmann, Cathleen; Schneider, Manfred; Rudolph, Michael; Reszka, Regina

CORPORATE SOURCE: Group Drug Targeting, Berlin-Buch, Max Delbruck Center for Molecular Medicine, Robert-Rossle-Strasse 10, Berlin, D-13125, Germany

SOURCE: International Journal of Pharmaceutics (1998), 162(1-2), 143-157

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 10 Apr 1998

AB A novel cationic amphiphile consisting of a hydrophobic 1,3-dioleoylglycerol moiety and a pos. charged spermine head group, 1,3-dioleoyloxy-2-(N5-carbamoylspermine)propane (DOCSPER), has been prepared. Based on natural occurring materials, DOCSPER is susceptible to metabolic degradation and a promising agent for delivery of therapeutical genes in vivo. In aqueous solns. this lipospermine spontaneously forms liposomes with a size of about 20-100 nm. Liposomes composed of DOCSPER and the helper lipid dioleoylphosphatidylethanolamine (DOPE) were several hundred nm in size. DOCSPER liposomes were tested for their ability to transfect the rat glioblastoma cell-line F98, the rat colon carcinoma cell-line CC531, the T-cell line Jurkat and the human mamma tumor cell-lines MCF-7 and MaTu. Transfectability and toxicity of liposomes prepared with DOCSPER were compared with the Lipofectin reagent. Toxicity was significantly lower and transfection efficiencies were similar compared to Lipofectin. Lipid/DNA complex formation was controlled by turbidity measurements allowing easy determination of optimal lipid/DNA ratio for transfection.

IT 203188-43-6P

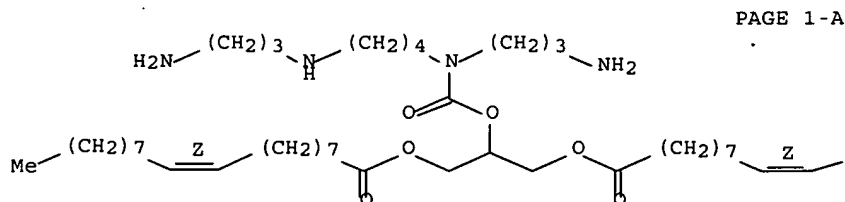
RL: BPR (Biological process); BSU (Biological study, unclassified);
PEP (Physical, engineering or chemical process); PRP (Properties);
SPN (Synthetic preparation); BIOL (Biological study); PREP
(Preparation); PROC (Process)

(preparation and characterization of a new lipospermine for gene delivery into various cell-lines)

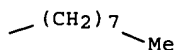
RN 203188-43-6 HCAPLUS

CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



PAGE 1-B



IT 203188-54-9P

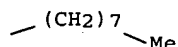
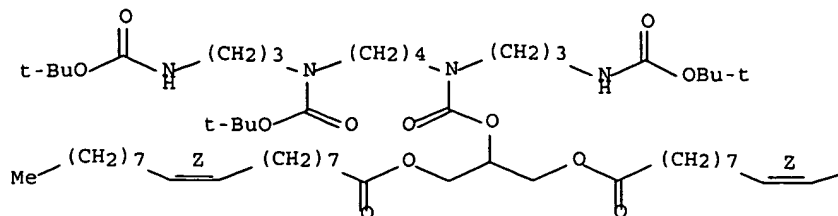
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)

(preparation and characterization of a new lipospermine for gene delivery into various cell-lines)

RN 203188-54-9 HCAPLUS

CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L23 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:184738 HCAPLUS Full-text
DOCUMENT NUMBER: 141:309461

TITLE: Structural effects of amphiphiles on *Candida rugosa* lipase activation by freeze-drying of aqueous solution of enzyme and amphiphile
AUTHOR(S): Mine, Yurie; Fukunaga, Kimitoshi; Samejima, Ken-Ichi; Yoshimoto, Makoto; Nakao, Katsumi; Sugimura, Yoshiaki

CORPORATE SOURCE: Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Yamaguchi University, Ube, 755-8611, Japan

SOURCE: Journal of Bioscience and Bioengineering (2003), 96(6), 525-528

CODEN: JBBIF6; ISSN: 1389-1723

PUBLISHER: Society for Biotechnology, Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 08 Mar 2004

AB Lipases co-lyophilized with water-soluble gemini-type amphiphiles were found to have high enzyme activity in nonaq. media without washing out of the amphiphile with anhydrous organic solvent. In this study, we obtained freeze-dried complexes of *Candida rugosa* lipase (CRL) with six water-soluble twin glucitol-headed amphiphiles bearing different types of hydrophobic tails, including newly synthesized ones, and their transesterification activity in organic solvent was evaluated. The results indicate that the increased enzyme activity upon CRL modification at 200 molar ratio of amphiphile/CRL, which are restricted to the ester-containing amphiphiles, is probably due to the surface activation by the interaction between ester-carbonyl of the amphiphile and Ph group of the tyrosine residue situated on the surface of the lid in the CRL.

IT 766549-39-7, BIG 2C120Gly 766549-40-0, BIG 2C120MeC

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(activation of *Candida rugosa* lipase using twin-headed

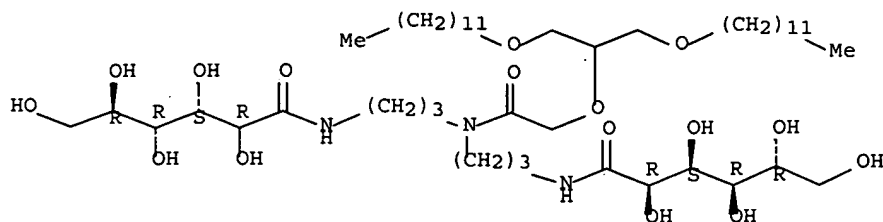
10/686374

amphiphiles of nearly the same hydrophobicity with different alkyl chains)

RN 766549-39-7 HCAPLUS

CN D-Gluconamide, N,N'-[[[2-(dodecyloxy)-1-[(dodecyloxy)methyl]ethoxy]acetyl]imino]di-3,1-propanediyl]bis-(9CI) (CA INDEX NAME)

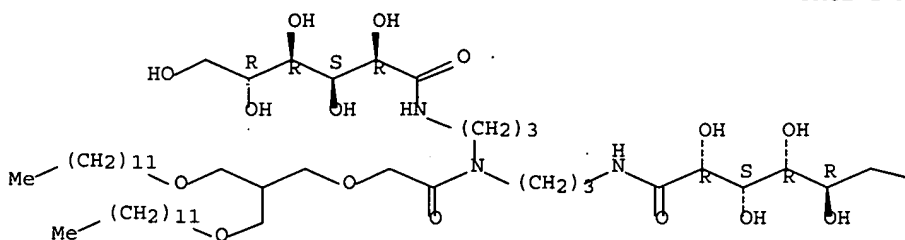
Absolute stereochemistry.



RN 766549-40-0 HCAPLUS

CN D-Gluconamide, N,N'-[[[3-(dodecyloxy)-2-[(dodecyloxy)methyl]propoxy]acetyl]imino]di-3,1-propanediyl]bis-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 1-B

— OH

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:102979 HCAPLUS Full-text

DOCUMENT NUMBER: 128:180582

TITLE: New cationic amphiphiles for liposomal gene transfer

INVENTOR(S): Schneider, Manfred; Keil, Oliver; Reszka, Regina; Groth, Detlef

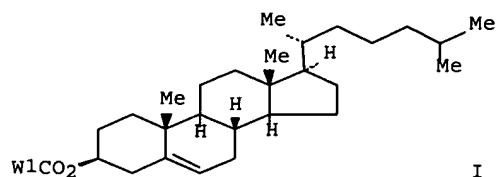
PATENT ASSIGNEE(S): Max-Delbrueck-Centrum fuer Molekulare Medizin,

10/686374

SOURCE: Germany
 Ger. Offen., 26 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19631189	A1	19980205	DE 1996-19631189	19960802
WO 9805678	A2	19980212	WO 1997-DE1669	19970801
WO 9805678	A3	19990225		
W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 923600	A2	19990623	EP 1997-936602	19970801
EP 923600	B1	20060621		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, FI				
JP 2000515861	T	20001128	JP 1998-507485	19970801
AT 330964	T	20060715	AT 1997-936602	19970801
US 6268516	B1	20010731	US 1999-230842	19990330
US 2002007073	A1	20020117	US 2001-898333	20010703
US 6489495	B2	20021203		
PRIORITY APPLN. INFO.:			DE 1996-19631189	A 19960802
			WO 1997-DE1669	W 19970801
			US 1999-230842	A3 19990330

OTHER SOURCE(S): MARPAT 128:180582
 ED Entered STN: 20 Feb 1998
 GI



AB Cationic amphiphiles, (R3COZCH2)CHYCOW [W = N{(CH2)nN+(R1)2R2}(CH2)mN+R1R2R3 2X-, CHR1NH2·HX, (CH2)nNHC(NH2):NH·HX; n = 2, 3, 4, 6, 8; m = 2, 3, 6, 8; R1 = H, Me, CH2CH2OH; R2 = H, Me, CH2CH2OH, (CH2)3N+(R1)3; R3 = linear, (un)saturated alkyl; Z = CH2, O, NH; Y = CH2, O, NH; X = Cl, Br, OAc, CF3CO2], and steroidal lipids I [W1 = N{(CH2)nN+(R1)2R2}(CH2)mN+(R1) 2R2 2X-, CHR1NHR2·HX, NH(CH2)mY] are described. Thus, cholesteryl lipid I·2HCl [W1 = CH(NH2)(CH2)3NH2] was prepared via reaction of Di-Boc-ornithine with cholesterol in CH2Cl2 containing DCC and DMAP followed by treatment with HCl in MeOH. These lipids are effective for liposomal gene transfer (data presented as graphs).

IT 203188-44-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-44-7 HCAPLUS

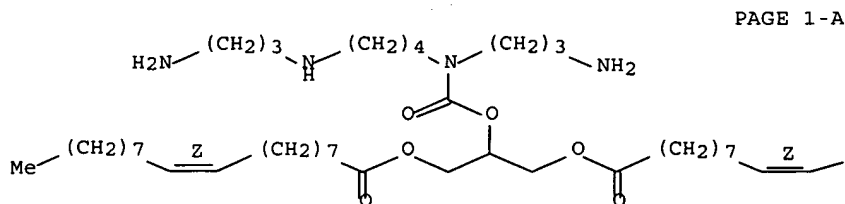
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

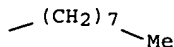
CRN 203188-43-6

CMF C50 H96 N4 O6

Double bond geometry as shown.

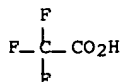


PAGE 1-B



CM 2

CRN 76-05-1
 CMF C2 H F3 O2



IT 203188-54-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-54-9 HCAPLUS

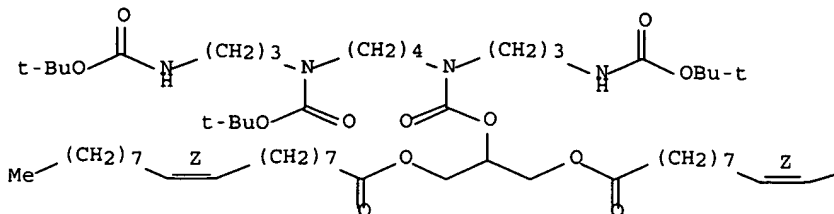
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-

10/686374

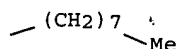
dimethylethoxy)carbonyl]-11-[[2-[[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-
[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-,
bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L23 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2002:12690 USPATFULL Full-text

TITLE: Novel cationic amphiphiles for liposomal gene transfer

INVENTOR(S): Schneider, Manfred, Wuppertal, GERMANY, FEDERAL
REPUBLIC OF
Keil, Oliver, Wuppertal, GERMANY, FEDERAL
REPUBLIC OF
Reszka, Regina, Schwanebeck, GERMANY, FEDERAL
REPUBLIC OF
Groth, Detlef, Ferch, GERMANY, FEDERAL REPUBLIC
OF

PATENT ASSIGNEE(S): Max-Delbruck-Centrum fur molekulare Medizin,
Berlin, GERMANY, FEDERAL REPUBLIC OF (non-U.S.
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002007073	A1	20020117
	US 6489495	B2	20021203
	US 2001-898333	A1	20010703 (9)
APPLICATION INFO.:	Division of Ser. No. US 1999-230842, filed on 30		
RELATED APPLN. INFO.:	Mar 1999, GRANTED, Pat. No. US 6268516 A 371 of		
	International Ser. No. WO 1997-DE1669, filed on 1		
	Aug 1997, UNKNOWN		

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1996-19631189	19960802
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	BRUCE LONDA, NORRIS, MCLAUGHLIN & MARCUS, P.A.,	

10/686374

220 EAST 42ND STREET, 30TH FLOOR, NEW YORK, NY,
10017

NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 477

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the synthesis of novel cationic, amphiphilic lipids and their application as gene transfer vehicles in vitro and in vivo. For this a series of different lipids (diglycerides, steroids) were synthesized by modification with variable cationic molecules (amino acids, biogenic amines). Compounds of this kind are, due to their capability of producing complexes with polynucleotides (DNA, RNA, Antisense oligonucleotides, ribozymes etc) suitable as vectors for gene transfer (transfection).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 203188-44-7P

(preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-44-7 USPATFULL

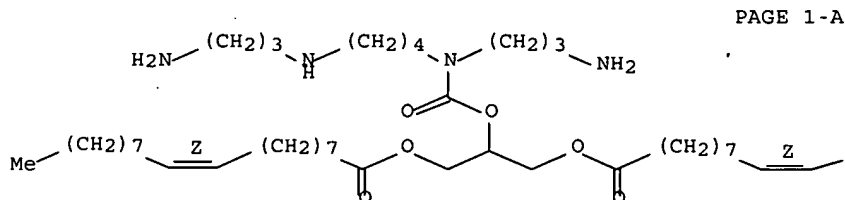
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

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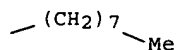
CRN 203188-43-6

CMF C50 H96 N4 O6

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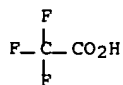
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 203188-54-9P

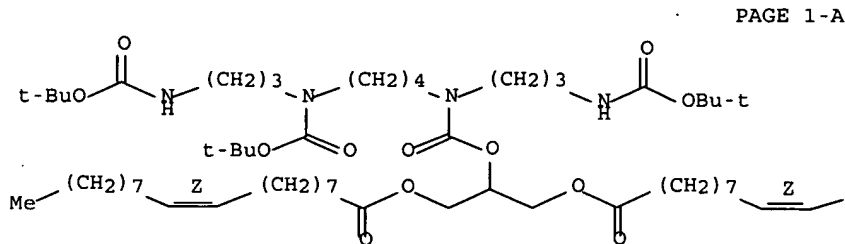
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(preparation of new cationic amphiphiles for liposomal gene transfer)
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RN 203188-54-9 USPATFULL

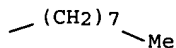
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



PAGE 1-A

PAGE 1-B



L23 ANSWER 8 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2001:121623 USPATFULL Full-text

TITLE: Cationic amphiphilic lipids for liposomal gene transfer

INVENTOR(S): Schneider, Manfred, Wuppertal, Germany, Federal Republic of
Keil, Oliver, Wuppertal, Germany, Federal Republic of
Reszka, Regina, Schwanebeck, Germany, Federal Republic of
Groth, Detlef, Ferch, Germany, Federal Republic of

PATENT ASSIGNEE(S): Max-Delbrück-Centrum für Molekulare Medizin,
Germany, Federal Republic of (non-U.S.
corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6268516	B1	20010731	
	WO 9805678		19980212	
APPLICATION INFO.:	US 1999-230842		19990330	(9)
	WO 1997-DE1669		19970801	
			19990330	PCT 371 date
			19990330	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1996-19631189	19960802
DOCUMENT TYPE:	Utility	

FILE SEGMENT: GRANTED
 PRIMARY EXAMINER: Badio, Barbara P.
 LEGAL REPRESENTATIVE: Norris, McLaughlin & Marcus
 NUMBER OF CLAIMS: 3
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
 LINE COUNT: 450

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the synthesis of novel cationic, amphiphilic lipids and their application as gene transfer vehicles in vitro and in vivo. For this a series of different lipids (diglycerides, steroids) were synthesized by modification with variable cationic molecules (amino acids, biogenic amines). Compounds of this kind are, due to their capability of producing complexes with polynucleotides (DNA, RNA, Antisense oligonucleotides, ribozymes etc) suitable as vectors for gene transfer (transfection).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 203188-44-7P

(preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-44-7 USPATFULL

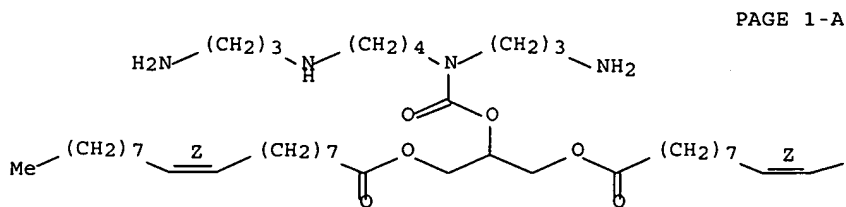
CN 9-Octadecenoic acid (9Z)-, 2-[[[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]carbonyl]oxy]-1,3-propanediyl ester, triis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

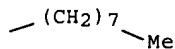
CRN 203188-43-6

CMF C50 H96 N4 O6

Double bond geometry as shown.



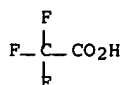
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



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IT 203188-54-9P

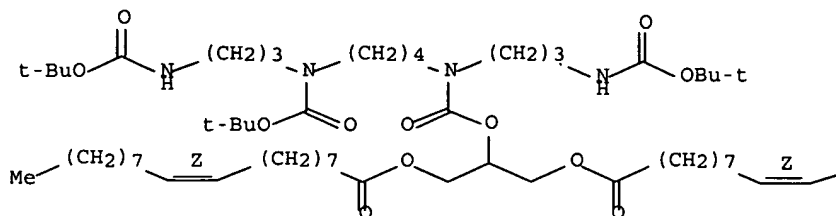
(preparation of new cationic amphiphiles for liposomal gene transfer)

RN 203188-54-9 USPATFULL

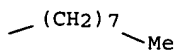
CN 2,6,11,15-Tetraazahexadecanedioic acid, 6-[(1,1-dimethylethoxy)carbonyl]-11-[[2-[[[(9Z)-1-oxo-9-octadecenyl]oxy]-1-[[[(9Z)-1-oxo-9-octadecenyl]oxy]methyl]ethoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



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